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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/608,077	06/30/2003	Paul D'Angio	9516-034-999	7850

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EXAMINER	
ROBERTS, LEZAH	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 04/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/608,077	D'ANGIO ET AL.	
	Examiner	Art Unit	
	Lezah W. Roberts	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *January 6, 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *A and B*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This office action is a response to the amendment filed January 6, 2006.

The office action is made FINAL.

New Matter

The amendment filed January 6, 2006 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the Applicant uses the term direct blend, but it is not defined or even disclosed in the specification.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claims

Claim Objections

The disclosure was objected to because of the following informalities: on page 5 of the specification, applicant uses # 0 for capsule size when disclosing the 50 mg capsule invention. It is believed this should read # 4 capsule.

Appropriate correction is required.

The Applicant has corrected the error and the objection has been withdrawn.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 24 is rejected under 35 U.S.C. 103(a) as being unpatentable over Andrulis *et al.* and Gennaro.

The applicants argue the claim is not obvious and discussed the difficulties of formulating a dosage form that is effective as well as smaller.

The examiner recognizes the arguments but they are not persuasive. The claim is broad and reads on all carriers. The disclosure by applicant discusses carriers that may be used and does not limit the carriers used (page 9), leading one to believe that all pharmaceutical carriers may be utilized in the invention. The applicant argues none of the cited references, or prior art teach using a size 4 capsule comprising 50 mg of thalidomide and 74 mg of carrier. The applicant states in its disclosure any size capsule can be used in the invention. The preferred capsules of the invention are of size #0, #2

or #4 (page 11, line 7). The prior art also teaches any size capsule can be used within its disclosure. It would be of benefit if there were a side by side comparison using different carriers of the claimed weight to determine if they all fit in the size 4 capsule, because the claim reads on all carriers. There is lack of support for the claim. The applicant's disclosure also lacks support for a 50 mg capsule. The disclosure gives a formulation for a 50 mg capsule but it is that of a prior art formulation. Therefore the argument is not persuasive.

Secondly, the applicant argues the formulation recited by claim 24 could not have been made by simply reducing the amount of carrier used for known formulations and gives reasons such as flow and bioavailability. Once again the claims read on all carriers, therefore it is assumed all carriers including those of past formulations would work in the formulation of claim 24. It would benefit the applicant to be more specific in what type of carrier and the characteristics of the carrier may be used in the composition. This is not stated in the claims or the disclosure. Applicant's argument is not persuasive.

To address the applicant's third issue, again the claim is broad therefore it reads on the formulation of Andurlis because the applicant does not recite a specific carrier or group of carriers with specific properties. The third argument is not persuasive.

Although the Applicant's argue there were unexpected results the claim is still broad and does not only encompass the applicant formulation but all formulation with that amount of carrier and thalidomide whether it has high bioavailability or not. The claim would be more acceptable if it is was more specific and the unexpected result was

disclosed in the specification. As it stands the formulation for 50 mg thalidomide capsules are not disclosed and have no support within the specification.

If the Applicant amended the claims to a narrower scope such as specifically naming the carrier, the claims would be in better shape for possible allowance.

Accordingly, the rejection stands.

2) Claims 25-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Andrulis, Jr. *et al* and Gennaro as applied to claim 24 above, and further in view of Govindarajan *et al.*

Claim 25-28 teaches a single unit dosage form of thalidomide comprising or about 50 mg of thalidomide, about 74 mg of carrier which is pre-gelatinized corn starch, and about 1 mg magnesium stearate to make a composition weighing about 125 mg in a size 4 capsule (40 : 59.2 : 0.8, ratio).

The applicant argues the claims cannot be obvious because they depend from claim 24. The argument is recognized but is unpersuasive. Govindarajan *et al.* discloses pre-gelatinized starch and said binders being present from about 50 to 99 weight percent in pharmaceutical compositions which encompasses the 60% which is the amount of the instant claims' percentage. It would be obvious to vary the amounts of starch to the desired to achieve the desired property. This is supported by In re Aller 105 USPQ 233, 235 (CCPA 1955), which states, normally, changes in result effective variables are not patentable where the difference involved is one of degree, not of kind; experimentation to find workable conditions generally involves the application of no

more than routine skill in the art. It is the burden of the Applicant to show the amount of starch incorporated was more involved than just trial and error, which the Applicant does not seem to do for the case of 50 mg thalidomide capsules.

To make the claims in possible condition for allowance, the Applicant could make claim 25 into an independent claim. It would also support the claim by using a side by side comparison within the specification to show another carrier of the same weight as the starch would not necessarily fit into a size 4 capsule with 50 mg of thalidomide. It would also be beneficial to discuss why the starch is unique.

The rejection stands.

3) Claims 29-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Andrulis, Jr. *et al* and Gennaro as applied to claims 24-28 above, and further in view of Baker *et al.* and Teo *et al.*

Claim 29-30 teaches a single unit dosage of 100 mg of thalidomide and 250 mg of carrier, including magnesium stearate, in a size 2 capsule.

The Applicant argues one cannot arbitrarily adjust the amount of carriers and expect the resulting formulation to have properties comparable to the original formulation. In regards to this point, the Applicant does not reference bioavailabily or effectiveness in the claim. Claim 29 recites a capsule comprising 100 mg of thalidomide and 250 mg of a carrier, any carrier. The applicant also argues that one cannot adjust the amount of carriers to fit one's purpose yet the applicant is claiming any carrier. Applicant is arguing pharmacokinetics which is not encompassed by the claims. Clearly

the Applicant is not concerned with effectiveness of the formulation because the claims read on any carrier. The Applicant is proving in their argument any carrier cannot be used but is claiming any carriers clearly contradicting themselves. Furthermore the specification supports a 100 mg tablet, not a 100 mg capsule. The claims would be more likely in condition for allowance if the claims recited a specific carrier and characteristic of said carrier supported by the specification.

The rejection stands.

4) Claim 31 is rejected under 35 U.S.C. 103(a) as being unpatentable over Andrulis, Jr. *et al.* and Gennaro as applied to claim 24 above, and further in view of Scheffler et al.

Claim 31 teaches a single unit dosage form of about 200 mg of thalidomide and 297.5 mg of a carrier in the form of a size 0 capsule.

The applicant argue it is not obvious from the disclosed reference to make a 200 mg capsule of thalidomide. They also argue that one would not have had a reasonable expectation of successfully obtaining a single unit dosage form in a size 0 capsule comprising 200 mg of thalidomide and only 297.5 mg of a carrier with pharmacokinetic and other properties comparable with that of other thalidomide formulations. Once again Applicant discusses pharmacokinetics. The claim has no limit stating the pharmacokinetics it only states a carrier, once again any carrier. Andrulis, Jr. *et al.* used for an example "a gelatin capsule containing 200 mg of thalidomide" (column 10, line 30-31). If a capsule did have 200 mg of thalidomide and 297.5 of carrier to fit it into a

certain size carrier would fit the claim. The pharmacokinetics have no bearing on the claim. Therefore the arguments are not persuasive.

The rejection stands.

5) Claims 31-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Andrulis, Jr. *et al.*, Gennaro, and Govindarajan *et al.* as applied to claims 25-28 above, further in view of and Scheffler *et al.*

Claims 31-35 teach a single dosage unit containing about 200 mg of thalidomide, about 297.5 mg of carrier and about 2.5 mg of magnesium stearate for a total of about 500 mg in a size zero capsule.

The Applicant argues the claims are not obvious for the same reasons as claim 31 because they are dependent on 31. This argument is not persuasive.

Claim 31 is not allowable therefore its dependent claims are not allowable. The claims would be more in condition for allowance if the claims were more specific to a certain carrier such as the pregelatinized starch carrier.

Interview

In regards to the subject matter discussed in the interview, it was agreed certain amendments would be made as long as they did not introduce new subject matter. The claim recited direct blend, which is not supported by the specification.

Conclusion

The claims as it stands are rejected. Suggestion to put the claims in better condition for allowance includes limiting the claims to one specific carrier. Also a side by side comparison of thalidomide capsules comprising different carriers would support that all carriers at a particular weight would not fit into a certain size carrier.

For Example

Capsule size	Carrier	Thalidomide
0	X	X
0	X	X
1	X	X
2	X	X
3	X	X
4	X	X
5	X	X

This would show not all carriers at the same weigh could fit in a certain size capsule, which would support the claims. Also a disclosure of other carriers that would be encompassed by the claim would be beneficial. The current disclosure mainly supports pregelatinized starch.

In conclusion the rejections stand.

No claims allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lezah W. Roberts whose telephone number is 571-272-1071. The examiner can normally be reached on 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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